INVASIVE SINO NASAL ASPERGILLOSIS - DIAGNOSTIC CRITERIA

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ABSTRACT : *This study highlights the high incidence of fungal granulomas in our patients and to streess the need to differentiate the invasive Sinonasal aspergillosis from the non invasive ones because, the management of invasive Aspergillosis includes the administration of the potentially toxic drug, Amphotericin. The various diagnostic criteria used by us to identify the cases for systemic anti fungal treatment in addition to thorough local debridement are discussed.*

INTRODUCTION

The nose, with its moist environment and with sequestrated spaces in the form of para nasal sinuses provides an ideal environment for the growth of fungi. The two important fungal infections involved in invasive fungal sinusitis are Aspergillosis and mucromycosis. Sino nasal Aspergillosis is caused by three types of fungi, Viz :

Aspergillus fumigatus, Aspergillus flavus and Aspergillus niger.

Most of the cases seen in our series were Aspergilli. Two cases of mucormycosis were seen in our study. The mode of entry of fungal spores into the nose and PNS is by inhalation, through sinus filtulae and/or through the perforation of the maxillary sinus via root canal.

The predisposing factors for the fungal sinusitis are :
A) Local anatomical factors within the nasal architecture leading to osteomeatal or other regional obstruction resulting in a decrease in sinus ventilation and lowered PH.

B) Immuno compromised states such as :

1) Usage of intensive chemotherapy and broad spectrum antibiotics in malignancies especially hematological neoplasms.

2) Acquired Immuno deficiency syndrome (AIDS).

3) Long term cortico steroid therapy for various conditions.

4) Severe diabetes mellitus and chronic systemic illnesses.

Immuno compromised states predispose a patient to invasive aspergillosis and hence patient needs aggressive total treatment to prevent a fatal outcome. So, it is important to identify invasive Aspergillosis as early as possible and treat it with parenteral Amphotericin in addition to local clearance. No systemic drug other than Amphotericin till date has been proven to be useful in sino nasal aspergillosis. Apart from the immuno compromised states, the clinical indicators which suggest invasiveness are, any immuno compromised patient with sinusitis who has not responded to routine treatment, spiking fevers, shooting facial pain or paresthesias, thick mucous rhinorrhoea of unusual color, pale relatively insensitive turbinates, black insensitive tissue crusts, spread to surrounding structures like orbit and intra cranial extensions and necrosis or gangrene of turbinates.

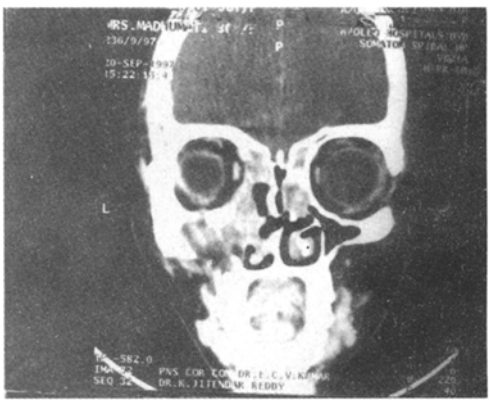

Fig. I : C. T. Scan of PNS - Showing erosion of medial wall of orbit and portions of maxillary sinus on left side and also involving opposite ethmoids by invasive fungal granuloma.

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Fig. II : C. T. Scan of PNS showing invasive fungal granuloma eroding anterior portion of skull base.

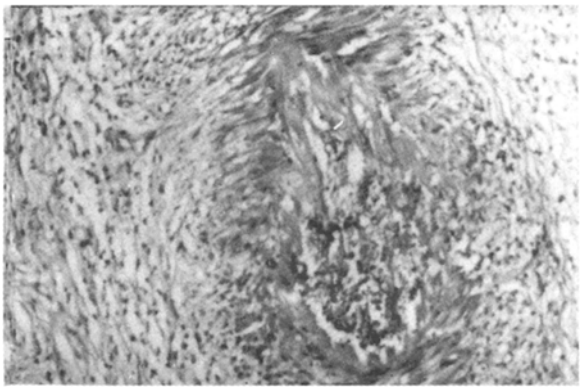

Fig. III : Histopathological findings of invasive sinonasal aspergillosis showing fungal thrombus in the vascular lumen.

Radiological features like bone destruction, specks of Calcification and irregular enhancement on contrast suggest aggressive nature of Aspergillosis.

The pathological features are very important and help to clinch the diagnosis of invasive Aspergillosis. These are :
A) Presence of mycelial elements on direct smear.
B) Large areas of tissue necrosis on histopathology.
C) Vascular invasion leading to thrombosis, aneurysm and ischaemia of surrounding tissues.

A positive culture of fungus from diseased tissues is a reliable guide for invasive aspergillosis.

Non invasive aspergillosis could be further classified into Allergic Sinusal Aspergillosis and colonising Aspergillosis or Aspergilloma.

Allergic sinusal Aspergillosis is characterized by the presence of mucinous material with entrapped eosinophils.

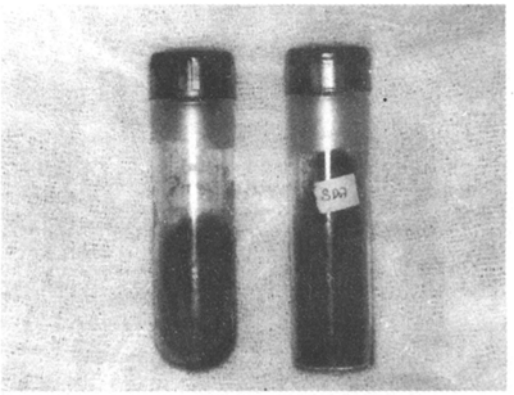

Fig. IV : Aspergillus grown in culture in a case of invasive sinonasal aspergillosis.

Aspergilloma (colonising type)shows a granulomatous appearance with or without colonies of fungi in the specimen.

MATERIALS & METHODS

During the period January, 93 to September, 97 (approx.,3 1/2 years), 95 cases of nasal polypectomies done were screened for fungal infections. In addition to the routine tests, the following investigations were done :

CT scan of para nasal sinuses with contrast study.

Histo-pathological study of all nasal polypi removed with routine haematoxylin and eosin stains and special stains like PAS (Periodic Acid Schiff stains) and GROCOTT'S silver methenamine stains, direct smear study of specimens of fungus and fungal culture. In severe infections, colonies of fungus are grown by a method called Abundant fungus method or repeated isolation of fungus and culture. It consists of growing Aspergillus from several specimens or several colonies from a single specimen.

Among the positive cases of fungal infections of PNS, the invasive ones which were identified by clinical radiological and histopathological criteria were subjected to a systemic antifungal treatment along with thorough local debridement. Allergic sino nasal Aspergillosis cases were treated with topical and systemic steroids and local clearance. Aspergillomas (colonising) type were subjected to a good local clearance and regular follow-up. amphotericin-B is the mainstay drug in the management of invasive aspergillosis. Before using the drug, its benefits have to be weighed against the untoward side effects & its cost is also very high. It can be given only in a

hospitalised patient. It is commercially available as Fungizone 50mg vials.

It is given parenterally by a slow I.V. infusion over a period of 6 hours. Test dose is increased by 5-10 mg/ day. It can be given daily or on alternate days, dose being 0.5-0.75 mg/kg body weight. Maximum permitted daily dose is 3-4 gms. Several months of therapy may have to be given depending on the necessity.

Amphotericin can cause several side effects in the form of fever, chills, rigors, headache, nausea, vomiting, thrombophlebitis etc. The potentially toxic effects are renal problems, cardiovascular toxicity, tinnitus, hearing loss, vertigo, visual disturbances, hepatic failure etc., and hence during the administration of amphotericin - B, there should be a constant monitoring of clinical & biochemical parameters.

RESULTS

Out of 95 cases of Sino nasal polyps studied, 18 cases showed associated fungal infections. Ages of the cases ranged from 18 years to 65 years, the peak incidence being in the 3rd and 4th decades.

Sex incidence showed that males were more common than females, the ratio being 12 males to 6 females. 10 patients belonged to the immuno suppressed category. Amongst these patients, 2 cases were of acute myeloid leukemia undergoing chemotherapy and 3 cases were of severe uncontrolled diabetes mellitus.

Based on the pathological study, all the proved sino nasal fungal infections showed evidence of Aspergillosis, except 2 cases which showed mucormycosis. Amongst 16 cases of Aspergillosis, 10 cases showed a positive culture growth. 3 types of Aspergilli were grown in culture, viz.

Aspergillus flavus	-	8 cases
Aspergilus fumigatus	-	6 cases
Aspergillus niger	-	2 cases

Patients were divided into 3 groups based on the clinical, radiological and pathological study, viz.

1. Allergic sinusal aspergillosis.
2. Aspergilloma (fungal ball or colonising type of Aspergillosis)
3. The invasive sino nasal aspergillosis which is the most important type amongst all with respect to management & prognosis.

The allergic type and colonising type were managed by conservative measures and they responded well to treatment. The invasive type was managed by systemic Amphotericin, thorough local debridement and control of underlying disorder. All the patients had responded to this treatment except one case of uncontrolled diabetes mellitus and renal failure who developed a dry gangrene of the paransal sinuses and spread to intracranial structures secondary to invasive sinonasal aspergillosis where there was a fatal outcome.

The thorough local debridement was done using Nasal Endoscopic procedures and open clearance wherever necessary.

DISCUSSION

The classification of Aspergillus infections as seen in various standard text books is complicated and confusing, the same condition being called by various names. There is no standard nomenclature, leading to a lot of misuse of terms.

Based on the various criteria viz., clinical, radiological and pathological aspects, we divided Aspergillus infections basically into 3 types viz., Allergic, Colonising and Invasive types. In addition to these, we have aspergilli residing as saprophytes in the nose without producing any reactions.

The classification of Aspergillosis helps in the effective management of the case. Amongst the 3 types, the invasive type requires a quick diagnosis and prompt management with systemic amphotericin and thorough local clearance to prevent a fatal outcome.

CONCLUSION

In conclusion, it is to be realised that invasive sino nasal aspergillosis is a serious and life threatening infection. It is especially significant in an immuno compromised patient.

A high degree of suspicion is needed to diagnose these cases at a very early stage. When a patient is diagnosed as having invasive Aspergillosis based on the various diagnostic criteria cited above, the management includes control of the underlying predisposing problem along with an aggressive and prompt treatment with systemic

amphotericin -B and thorough local debridement to save the life from a potentially fatal disease.

REFERENCES

1. Baydala L.T., Yanofsky R.,Akabutu J., Wenman W. N., (May15 1988) :Aspergillosis of the nose and paranasal sinuses in immuno compromised children , Can Med Assoc J (Canada); 138(10) p 927 - 8, JSSN : 0008-4409.
2. Becelli R., Sassana P. Liberatore G. M., Arcese W. (Apr, 1995) : Surgical and local treatment in a case of fungal sinusitis in a patient with bone marrow aplasia, Minerva Stomatol (Italy) ; 44(4) p171-4, ISSN : 0926 - 4970.
3. Khoo S. H., Denning D. W. (Jan-Feb 1995) : Cure of chronic invasive sinus aspergillosis with oral saperconazole J Med Vet Mycol (England), 33 (1) p 63-6, ISSN : 0268 -1218.
4. Palacio C., Acebedo G., Lopez A., Jodar J. M., (Oct, 1994) : Remission of invasive sinusal and pulmonary aspergillosis with liposomal amphotericin B in a patient with chronic lymphatic leukemia following failure with conventional amphotericin, Sangre (Barc) (Spain), 39 (5) p 389-92, ISSN : 0036-4355.
5. Manso E., Montillo M., De Sio G., D. Amico S. (Sept 1994) : Value of antigen and anibody detection in the serological diagnosis of invasive aspergillosis in patients with hematological malignancies., Eur j Clin Microbiol Infect Dis (Germany), 13 (9); p756-60; ISSN : 0934 - 9723.
6. Bonfils P. : Trotouk J. (1989) : Mucormycosis of the face associated with aspergillosis in the diabetic patient. Diagnostic and therapeutic considerations.. Ann Otolaryngol Chir Cervicofac (France) ; 106 (6); p327-9; ISSN : 0003-438X.
7. Peteron D. E., Schimpff S. C. (1989) : Aspergillus sinusitis in neutropenic patients with cancer : A review. Biomed Pharmacother (France), 43 (4) ; p307-12 ISSN : 0753-3322.
8. Antoine G. A., Gates R. H.,(Jan - Feb 1988) : Invasive aspergillosis in a patient with aplastic anemia receiving amphotericin B. Head and Neck Surg. (United States); 10(3) p199-203 ; ISSN : 0148-6403.
9. Talbot G. H., Huang A., Provencher M. (Mar - Apr 1991) : Invasive aspergillus rhinosinusitis in patients with acute leukemia. Rev Infact Dis (United States) : 13 (2) : p219-32 ; ISSN : 0162 - 0886.
10. John S. Rubin, Alexabder B. Glickman (1994) : Invasive fungal sinusitis in the immunocompromised Host. Cliniguide to Fungal infections ; p1-8, ISSN : 1051-4945.